UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,662	04/27/2001	Eva Raschke	8325-0012	9004

20855 7590 06/25/2009

ROBINS & PASTERNAK
1731 EMBARCADERO ROAD
SUITE 230
PALO ALTO, CA 94303

EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
06/25/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/844,662	**Applicant(s)** RASCHKE ET AL.	
	Examiner ROBERT M. KELLY	**Art Unit** 1633	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 10 June 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☒ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): none.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *none*.
   Claim(s) objected to: *none*.
   Claim(s) rejected: *57 and 68-71*.
   Claim(s) withdrawn from consideration: *91,96-102*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☒ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). Notice of Non-Comp.
13. ☐ Other: _____.

/Robert M Kelly/
Primary Examiner, Art Unit 1633

Continuation of 3. NOTE: Claim 1 has been amended from "non-naturally zinc fingers" which contain certain characteristics, to "a zinc finger" which contains certain characteristics. Such requires further considerations for whether or not Applicant possessed the proposed-broadened genera with characteristics. Also, such proposed amendment requires further search and examination considerations. Finally, as noted in the attached Notice of Non-Compliant amendment, the proposed amendment does not cancel the withdrawn claims, which were elected with traverse, and this Application, not being a 371 of a PCT application, does not allow such without a petition to rejoin non-elected inventions or such other action as required.

Continuation of 11. does NOT place the application in condition for allowance because: With regard to the specific proposed-amendment, the written description/new matter rejections are not overcome by the proposed amendment, because the amendment is not entered. With regard to other arguments concerning this specific proposed amendment, the argument that the 7 amino acids are designed and/or selected is not persuasive, as the claims do not require that "the 7 amino acids of the recognition helix are designed and/or selected, and the only non-naturally-occuring subject matter described as possessed is that of non-naturally occuring amino acids, which again are not claimed. The broad argument for not being required to have literal verbiage is not persuasive because there is no requirement so-made; the examiner has argued that there is no description commensurate at all, and at best, the use of non-naturally occuring amino acids would be within the scope of the claim. While no literal description is required, the genera must be adequately described for its breadth as possessed, rather than obviousness-type support. With regard to interpretation of the claims in light of the disclosure, such misses the point. The claims are given their broadest reasonable breadth, and interpretations in light of the disclosure do not change this fact. Applicant's claims are not possessed by Applicant, for their full generically claimed embodiments. Applicant argues that the claims, read in light of the specificiation mean that the sequences which are "non-naturally occuring" are those that are designed or selected. Such is not persuasive, and well drawn to the point at hand. Does this description suffice for modifying the broad terminology of "non-naturally occuring"? The Examiner does not find it to be so-modifying of the broadest reasonable interpretation. Applicant has not provided a definition of "non-naturally occurring" to be those sequences which are designed or selected, but instead attempts to modify the meaning of words with plain meaning. It would appear that Applicant did not contemplate in their specification that design/modification could yield anything but non-naturally occuring zinc fingers/sequences. However, Applicant, not being cognizant of such, specifically means that Applicant did not possess the breadth of what Applicant is claiming. If Applicant wants to limit the claim to those that are designed or selected, it would appear that Applicant should claim seuqences that are designed or selected. However, attempting to subvert the plain meaning of words, to remove their black-and-white meaning, is antethetical to plain english, and hence, is not allowed. While Applicant may be their own text, Applicant has not provided a definition, and if such definition removed the plain meaning of the words, then it would be improper anyway. Applicant argues that there exists much art to demonstrate possession of selection/designing sequences. Such is not persuasive. It has nothing to do with the rejections. With regard to the rejection for anticipation, Applicant argues, citing the specificaiton, that Choo does not actually form complexes with cellular chromatin. Such is not persuasive. Choo is not required to state that they did it, but only teach that it can be done. Clearly, Example 5 teaches that "In addition to repressing the expression of the gene, the protein can be used to diagnose the precise point mutation present in the genomic DNA, or more likely in PCR amplified genomic DNA, without sequencing. It should therefore be possible, without further inventive activity, to design diagnostic kits for detecting (e.g. point) mutations on DNA. ELISA-based methods should prove particularly suitable." Moreover, with regard to Applicant's argument that cites a paragraph in Example which states "The selective stimulation of transcription indicates convincingly that highly site-specific DNA-binding can occur in vivo. However, while transient transfections assay binding to plasmid DNA, the true target site for this and most other DNA-binding proteins is in genomic DNA. This might well present significant problems, not least since this DNA is physically separated from the cytosol by the nuclear membrane, but also since it may be packaged within chromatin." to argue that Choo does not enable binding cellular chromatin. However, such argument is selective reading of the example, which must be context. In fact, the same example demonstrates that this question is overcome, by performing experiments to demonstrate that it can bind cellular chromatin. In fact, further on, after a consideration of the results in the same Example 3, Choo states "In summary, the inventors have demonstrated that a DNA-binding protein designed to recognise a specific DNA sequence in vitro, is active in vivo where, directed to the nucleus by an appended localisation signal, it can bind its target sequence in chromosomal DNA. This is found on otherwise actively transcribing DNA, so presumably binding of the peptide blocks the path of the polymerase, causing stalling or abortion. The use of a specific polypeptide in this case to target intragenic sequences is reminiscent of antisense oligonucleotide- or ribozyme- based approaches to inhibiting the expression of selected genes (Stein & Cheng 1993 Science 261, 1004-1012). Like antisense oligonucleotides, zinc finger DNA-binding proteins can be tailored against genes altered by chromosomal translocations, or point mutations, as well as to regulatory sequences within genes. Also, like oligonucleotides which can be designed to repress transcription by triple helix formation in homopurine-homopyrimidine promoters (Cooney et al., 1988 Science 245, 725-730) DNA-binding proteins can bind to various unique regions outside genes, but in contrast they can direct gene expression by both up- or down- regulating, the initiation of transcription when fused to activation (Seipel et al., 1992 EMBO J. 11, 4961-4968) or repression domains (Herschbach et al., 1994 Nature 370, 309-311). In any case, by acting directly on any DNA, and by allowing fusion to a variety of protein effectors, tailored site-specific DNA-binding proteins have the potential to control gene expression, and indeed to manipulate the genetic material itself, in medicine and research" Hence, it would appear that Choo literally teaches exactly the opposite of Applicant's argument. Still further, this same reference teaches screens and kits to bind new target sequences, which, taken in context of the paragraph the Examiner has just cited, means that these compositions must be enabled for binding cellular chromatin as the target sequence. Hence, not only is Choo anticipating the present claims with respect to the specific zinc finger cited, but, due to the breadth of claims, it must be enabled for similar binding complexes in cellular chromatin. With regard to the rejections under obviousness, Applicant argues that Choo does not describe or demosntrate the claimed complexes, and hence, it cannot be obvious. Such is not persuasive. First, Choo teaches that can be made. Second, as evidenced by the claims, the claimed target-sequence bound zinc fingers are obvious. Third, as demonstrated above, Applicant's arguments utilize text out of context. Applicant argues that oher laboratories after Choo's disclosure argue that willful and specific regulation of genes with designed transcription factors has remained an unmet challenge in biology (p. 13). Such is not persuasive because Choo teaches that they can bind the sequences. Moreover, Choo recognizes that binding the native sequence must be accounted for, because it can block transcription of such with their specific mutant, and kill the cell. How does this not demonstrate that for this factor in specific, it will not work? Moreover, given the specifications claims, it must neessarily be enabled for binding any target sequence, which clearly includes target sequences in cellular chromatin, as demonstrated above. Applicant

argues Beerli, stating that complete lack of predictability using zinc fingers to bind endogenous genes based on studies such as Choo's, and specifically quoting "This is the first time we've been able to show that these designed transcription factors work on real genes and real chromosomes, not genes of binding sites that have been introduced into cells,". Such is not persuasive. Applicant has not cited this in an IDS because it would be denied consideration, as Applicant has not paid the fee for consideration, nor has Applicant stated good and sufficient reasons why it was not presented earlier. Hence, it is not considered. However, on the basis of the argument alone, Applicant does not provide the quotations in context, and as evidenced above, Applicant has problems with taking text out of context. Secondly, Applicant does not provide the quotations with regard to " complete lack of predictability", and hence it is not commented upon. Thirdly, Applicant's quotation which is provided states that it was the first time they were able to show the binding, not that the Art has never been able to show an inability to bind. Fourthly, the Examiner cannot question the validity of an issued patent, and Choo's patent claims require enablemnet for binding target DNAs in cellular chromatin. Fifthly, there is no basis from Applicant's argument to determien that the zinc fingers are in any way related to Choo's, but Choo by must of necessity be enabled. Hence, even if the amendment were entered, the various rejections would be maintained.